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In the Specification

Please amend paragraphs [0161], [0162], [0167], [0169], and [0174] of the Specification as follows:

[0161] ~~RT±PCR~~ **RT-PCR** The exon 5 (sense primer 5'-GAC TGT ATG GAT GTTCTG TCA G-3'; SEQ ID NO:65) and exon 6 (antisense primer 5'-ATT TGTCCT GGC AGA CGA AGC A-3'; SEQ ID NO:66) were designed on the basis of published RAR β 2 transcript (de The' et al., 1990; van der Leede et al., 1992) and used to amplify 50 ng of DNase treated total RNA using the Superscript One-StepRT± PCR System (Life Technologies). RT± PCR with actin primers (sense primer 5'-ACC ATG GAT GAT GAT ATCG-3'; SEQ ID NO:67 and antisense primer 5'-ACA TGG CTG GGG TGTGA AG-3'; SEQ ID NO:68) was used as an internal RNA control.

[0167] **The RAR β 2 promoter is methylated in breast cancer cell lines independently of their ER status and RA-inducibility** RAR transcription was first tested in a panel of breast cancer cell lines grown in the absence of exogenous RA, by reverse transcriptase-PCR (RT ± PCR), using primers encompassing exons 5 and 6 (de The' et al., 1990; van der Leede et al., 1992; Toulouse et al., 1997). Under these conditions, only one cell line, Hs578t, produced a detectable 256 bp ~~RT±PCR~~ **RT-PCR** product. Thus, previous reports were confirmed that RAR β gene expression is down regulated/lost in breast cancer cell lines. Growing cells in the presence of RA can assess the distinction between down regulation and loss. As previously reported (Swisshelm et al., 1994; Liu et al., 1997; Shang et al., 1999), we observed induction of RAR β expression and growth inhibition in T47D, MDA-MB-435, MCF7 and ZR75-1 cell lines treated for 48 h with 1 μ M RA, but not in the MDA-MB-231 and MDA-MB-468 cell lines.

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[0169] The HDAC inhibitor TSA can reactivate RAR β expression in RA-resistant cells; demethylation of the RAR β 2 promoter is not an absolute requirement for RAR β reactivation The chromatin status at a given locus can be dynamically influenced by the degree of acetylation/deacetylation due to HAT/HDAC activities. Absence of RAR β regulatory factors, like RAR α , as well as DNA-methylation, can contribute to pattern chromatin modifications at RAR β promoter in RA-resistant cell lines. One of these cell lines, MDA-MB-231, lacks RA-inducible RAR α activity (Shao et al., 1994) and displays a RAR β 2 methylated promoter. A subsequent study was designed to probe indirectly whether the level of HDAC at RAR β 2 can influence RAR β expression, by testing the effect of TSA, a HDAC inhibitor on MDA-MB-231 cells (Yoshida et al., 1995). Cells were treated for 2 days, in the presence or absence of 100 ng/ml TSA alone, or in combination, with 1 μ M RA. By using ~~RT-PCR~~ RT-PCR, it was clear that, unlike cells treated with RA alone, cells treated with a combination of RA and TSA re-expressed RAR β mRNA. Under the same experimental conditions, 100 ng/ml TSA alone, or in combination with 1 mM RA, produced 77 and 92% growth inhibition, respectively. Treatment with 1 μ M RA alone did not affect significantly growth inhibition (52%). By MSP analysis, it was assessed that RAR β expression was restored in the presence of a methylated RAR β 2 promoter. This finding indirectly shows that global alterations of HDAC activity, generated by TSA in MDA-MB-231 cells, involved RAR β 2 resulting in RA-induced RAR β expression. Further, demethylation at RAR β 2 did not seem to be an absolute requirement for RAR β gene expression in MDA-MB-231 cells. Noteworthy, persistence of methylation at RAR β 2 was observed also in MCF7 cells where RAR β transcription could be restored in the presence of RA. Growth inhibition was observed in cells treated with TSA alone, or in combination, with RA. Very likely, RAR β along with TSA, a drug known to induce growth inhibition (Yoshida et al., 1995), contributed to the massive growth inhibitory effect that was observed.

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[0174] Methylation specific PCR (MSP) and sodium bisulfite DNA sequencing One μ g of genomic DNA was treated with sodium bisulfite²¹ and was analyzed for MSP using primer sets specific for methylated DNA: 5'-TTTAGCGGTGGCGTTCG-3' (sense; SEQ ID NO:69) and 5'-ATACGACTTCGAATCACGTA-3' (antisense; SEQ ID NO:70), and primers specific for unmethylated DNA: 5'-TTGGTTGGAAGTTGGGTG-3' (sense; SEQ ID NO:71), and 5'-AATACAACCTCAAATCACATAC-3' (antisense; SEQ ID NO:72) which yielded products of 183 and 213 bp respectively. Sodium bisulfite treated DNA was used to PCR-amplify the HOXA5 promoter region -97 to -303 bp, using the primers 5'-ATTTTGTTATAATGGGTGTAAT-3' (sense; SEQ ID NO:73) and 5'-AACATATACTTAATCCCTCC-3' (antisense; SEQ ID NO:74). The product was purified using a Qiagen PCR purification kit (Qiagen Corp.) and was sequenced using the sense primer with an ABI automated fluorescent sequencer according to the manufacturer's instructions.